REMARKS

Currently, claims 1-6 and 29-68 are pending in the present application. Applicant wished to express his gratitude to the Examiner for withdrawing the previous 35 USC 103(a) rejection. No new matter has been added as a result of the above amendments.

Rejection of claim 68 under 35 USC § 112, first paragraph

Claim 68 is rejected under 35 USC 112, first paragraph for lack of enablement. Applicant respectfully disagrees.

The Examiner states that while the specification enables the combination of amlodipine and atorvastatin metabolite it does not enable the further combination of endogenous and/or exogenous antioxidants. The Examiner continues and asserts that the "specification fails to provide information that would allow the skilled artisan to fully practice the invention without undue experimentation." The Examiner contends that the limitation "endogenous and/or exogenous antioxidants" is merely functional.

It is well known to those skilled in the art both endogenous and exogenous antioxidants. For example, pages 1177 - 1178 of Textbook of Medicine, Goldman, *et al.* (eds.), 21 ed., W,B, Saunders (Pub.), 2000, the entire teaching of which is incorporated herein by reference, discusses various antioxidants. Clearly, this illustrates that one skilled in the art can appreciate what is meant by antioxidants. (Applicant can supply a copy of the cited pages should the Examiner request.) Therefore, it is well within the scope of one skilled in the art to understand and employ the art recognized antioxidants as of the time the present application was filed. (See, MPEP § 2173.02.)

The Examiner articulates the concern that it is highly unpredictable in regard to combining the antioxidants with amlodipine and atorvastatin. It is well known and appreciated in the art that antioxidants, *e.g.*, vitamins A, C and E, can be taken without

serious side effects. In fact, the claim construction requires an "effective amount" of atorvastatin and amlodipine - consistent with the claim language, it is understood that the additional antioxidant ingredient would be an effective amount. In fact, claim 68 has been so amended. Antioxidants, such as those mentioned above, have known toxicity profiles. Nothing in the prior art suggests that these antioxidants used in combination with atorvastatin and amlodipine increase or exacerbates known toxicity.

Additionally, MPEP § 2111.01 clearly states that an applicant may use *functional* language which makes clear the boundaries of the subject matter for which protection is sought. (Also, see, *In re Swinehart*, 439 F.2d 210, 160 USPQ 226 (CCPA 1971).) Again, the term antioxidant is clearly understood by those skilled in the art and defines the boundaries of the invention.

In conclusion, both endogenous and exogenous antioxidants are well known to those skilled in the art at the time this current application was filed. The pharmacokinetics and dynamics of these antioxidants are well understood and suggest that in an effective, physiological amount will result in no prohibitive toxicity. The claimed invention indicates that these antioxidants will complement the atorvastatin/amlodipine combination. The prior art provides for sufficient detail on the pharmacology of the antioxidants as of the filing of this application. Therefore, the present specification is fully enabled with respect to 35 USC 112, first paragraph.

Moreover, it is axiomatic in patent law that if an independent claim (claim 63) defines allowable subject matter then the claims depending therefrom also define allowable subject matter. *In re* Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), and Hartness International, Inc. v. Simplimatic Engineering Co., 819 F.2d 1100, 1108, 2 USPQ2d 1826, 1831 (Fed. Cir. 1987). Given that the rejected claims depend from base claims and those independent claims define allowable subject matter, then the claims at issue must necessarily define allowable subject matter. The reasons for allowability of the base claims are set forth herein.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the present rejection.

Rejection of claim 68 under 35 USC § 112, second paragraph

Claims 2-3 and 58-59 are rejected under 35 USC 112, second paragraph for lack of enablement. Applicant respectfully disagrees.

The Examiner states that "the recitation, 'derivative of amlodipine' renders claims 2-3 and 58-59 indefinite." The Examiner continues, "the recitation, 'derivative of amlodipine' is not clearly defined in the specification. Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patent protection ..."

The term "derivative" is well understood by those skilled in the art. Moreover, it is well established that plain meaning is to be applied to any term within a claim. Derivative is defined in Webster's Universal College Dictionary, 1991, Random House, as "3. a chemical substance or compound obtained or regarded as derived from another substance or compound." The Dictionary of Scientific and technical Terms, 3rd ed., 1984, McGraw-Hill, defines derivative as " a substance that is made from another substance." It is not a terribly difficult concept to understand what derivative means. A derivative is a compound that is derived from a parent compound, *e.g.*, amlodipine. Claim 3 actually provides for an example of a derivative of amlodipine. The derivative is a salt derivative of amlodipine.

In conclusion, Applicant contends that the term "derivative" is not indefinite and that in fact, it is well understood by the skilled artisan. Hence, Applicant respectfully requests reconsideration and withdrawal of the present rejection.

Rejection of claims 1-6, 57-59 and 63-67 under 35 USC § 102(b)

Claims 1-6, 57-59 and 63-67 are rejected under 35 USC 102(b) as being anticipated by the Pfizer News, May 20, 1997. Applicant respectfully disagrees.

The Examiner contends that "Pfizer News discloses the combination of Norvasc also known as amlodipine besylate ... and Lipitor also known as atorvastatin calcium in their effective amounts for treating cardiovascular diseases ... Hydroxylated atorvastatin metabolite claimed herein is a metabolite of atorvastatin, which was necessarily produced in the patient's body upon ingestion of atorvastatin ... Thus, atorvastatin disclosed by the Pfizer News would anticipate hydroxylated atorvastatin metabolite." In the proffered argument, the Examiner cites Schering Corp. v. Geneva Pharmaceuticals, Inc., 68 USPQ2d 1760 (CAFC 2003).

The Court in Schering, in particular section II last paragraph, states "[a] skilled patent drafter, however, might fashion a claim to cover the metabolite in a way that avoids anticipation. For example, the metabolite may be claimed in its pure and isolated form, as in Kratz and Bergstrom, or as a pharmaceutical composition ..." Applicant has amended independent claims 1, 57, 63 & 64 to include the limitation "a substantially pure form of" hydroxylated atorvastatin metabolite. Support for this limitation can be found in the present specification, for example, on page 3, paragraph 7 which specifically discloses that the hydroxylated atorvastatin metabolites and their methods of preparation are shown in US Patent No. 5,385,929.

In light of the amendments made herein, Applicant considers the claims to define allowable subject matter and, therefore, respectfully requests reconsideration and withdrawal of the present rejection.

Rejection of claim 68 under 35 USC § 103(a)

Claim 68 is rejected under 35 USC 103(a) as being unpatentable over the Pfizer News, May 20, 1997 in view of Gilligan *et al.* (J. Amer College Card., 1994, 24(7), 1611-7. Applicant respectfully disagrees.

The Examiner refers back to argument put forth for the 102 rejection with respect to Pfizer News. However, the Examiner adroitly points out that the "News does not expressly disclose the combination therein further comprising an antioxidant." The

Examiner continues and states that "Gilligan et al. teaches that antioxidants such as Vitamin A, C, and E are known to be used in the treatment of hypercholesterolemia in humans." The Examiner concludes by stating "It would have been obvious to a person of ordinary skill in the art at the time the invention was made to further employ antioxidants such as Vitamin A, C, and E in the composition for treating ..."

In order to establish a *prima facie* case of obviousness, "there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references) must teach or suggest all of the claim limitations." M.P.E.P. §2143, see also, *In re* Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Moreover, it is axiomatic in patent law that if an independent claim defines allowable subject matter then the claims depending therefrom also define allowable subject matter. *In re* Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), and Hartness International, Inc. v. Simplimatic Engineering Co., 819 F.2d 1100, 1108, 2 USPQ2d 1826, 1831 (Fed. Cir. 1987). Given that the rejected claims depend from base claims and those independent claims define allowable subject matter, then the claims at issue must necessarily define allowable subject matter. The reasons for allowability of the base claims are set forth above.

There is no teaching or suggestion in the art cited to combine the composition of amlodipine/atorvastatin metabolite with one or more antioxidants, including any vitamin. Neither alone or in combination do the cited art teach or disclose the synergistic effect of using amlodipine and atorvastin metabolite in combination further in combination with an antioxidant. Without such teaching or suggestion, there can be no *prima facie* case of obviousness.

Moreover, Pfizer News fails to teach the atorvastatin metabolite, hence the all elements requirement is not met by this combination of cited art. (See above for a discussion of metabolite vs parent compound.)

The Examiner asserts that if one skilled in the art were to combine, there would be a reasonable expectation of obtaining an "additive therapeutic effect." Importantly, claim 63 requires a "synergistic" effect which is clearly distinct from additive. One skilled in the art appreciates the difference between "additive" and "synergistic" and would consider the two terms synonymous. Further, there is no suggestion, data or alike which suggests that combining Pfizer News with Gilligan would result in even an additive therapeutic effect.

In conclusion, Applicant contends that claim 68 defines allowable subject matter and, therefore, respectfully requests reconsideration and withdrawal of the present rejection.

Double Patenting

Applicant asserts that the pending claims are patently distinct from both US Application No. 10/637,781 and 10/214,058. The claimed subject matter in Applicant's pending application require that the combination of amlodipine and atorvastatin metabolite result in a synergistic therapeutic effect while the two cited applications do not. Further, Applicant's claimed invention recites an hydroxylated atorvastatin metabolite while the two cited applications do not. Hence, Applicant contends that his claimed invention is patentably distinct from both of the cited applications.

In conclusion, in view of the above amendments and remarks, Applicant respectfully requests the Examiner find the pending claims in condition of allowance and, therefore, issue a Notice of Allowance.

Although no fees are required, please charge any underpayment of fees to or credit any overpayment of fees to Deposit Account No. 03-2410.

The Examiner is invited to call the undersigned attorney at (617) 854-4237 should he determine that a telephonic interview would expedite prosecution of this case.

Respectfully submitted,

S/

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